

# Review of: "Targeting Cancer Cell Signaling Using Precision Oncology Towards a Holistic Approach to Cancer Therapeutics"

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Potential competing interests: No potential competing interests to declare.

The topic of review by M. Kumar is overall of interest, however requires careful revision to render it appealing for publication.

1. The introduction is too long, providing a lengthy historical excursus of the research and fight of cancer. This is not needed. It should be re-written, with focus on molecular features of cancer and their targeting.
2. Table 1.: the title needs to be changed since the listed markers are not biomarkers, but molecules expressed in tumor cells with over-expression in cancer stem cells.
3. It is not clear in paragraph 3. the link between cancer stem cells and immune infiltration of tumors. The author jumped from one topic to the other without any logical connection.
4. the long list of mutated genes described in tumors should be categorized by functions and moreover type of tumors. It will help to add a Table with the descriptions of the mutations and the associated type of tumors.
5. Overall a lengthy description of molecular alterations/mutations in cancer cells is providing, however the connection with actionable drugs is missing. Moreover, the described molecular pathways are commonly aberrant in multiple tumor types. It is not clear their relevance for the precision medicine. This point should be made clear, providing also examples.
6. paragraph 6. the sentence "It has been widely applied in precision medicine-based healthcare practices and is found to be greatly useful in medical oncology practice" is not correct. the usage of AI to precision medicine is still at the birth phase and its translation in therapeutic treatments is still under development.
7. The part dedicated to existing therapeutic intervention is missing the appropriate description of immunotherapy, including the rationale and the most recent achievements.
8. The author describes the role of antagonist CTLA-4 mAb as immunotherapy approach, but do not describe PD-1/PD-L1 signaling and the blockade with mAbs leading to significant improvement of overall survival in patients with different types of cancer. Since the blockade of CTLA-4, several immune checkpoint blockade agents have been developed, that should be described. Moreover, the combination of immunotherapeutic approaches as well as the usage of the mutanome for the development of patients' tailored cancer vaccines should be described. This represents a good fit for the topic of precision medicine.
9. Overall, the topic of the review is of interest, however the text results in a lengthy and generic description. The author

should focus the manuscript to the scope of the review, as in the title and in the abstract, and limit the description of molecular pathways, genomic platforms and therapeutic intervention that meet the scope of the development and progress of precision medicine for cancer patients.